1050-42 **Reperfusion Therapy With Either Intravenous Thrombolysis or Primary PTCA In Elderly Patients Is Beneficial: One-Year Results From a Nationwide French Registry of Acute Myocardial Infarction**

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Background: The role of early reperfusion therapy at the acute stage of MI in elderly patients is debated. Aim and Methods: The aim of this study was to analyze the prognostic role of reperfusion with IV thrombolysis or primary PTCA in the nationwide USIK database, which prospectively included all pts admitted to a CCU for an AMI in France in November 1995. For the purpose of the present study, only patients admitted within 24 hours of AMI and with one-year follow-up available were included. Results: Of the 1,838 patients included, 785 were > 70 years old, of whom 225 (29 %) had early reperfusion therapy with thrombolysis (n=173) or primary PTCA (n=52). Patients treated with early reperfusion had a baseline profile that differed from that of patients treated conventionally: women (31 % vs 50 %, p < 0.001), admission within 6 hours of symptom onset (84 % vs 54 %, p < 0.001), history of systemic hypertension (48 % vs 60 % p < 0.002), history of stroke (5 % vs 11 %, p < 0.01), peripheral arterial disease (8 % vs 18 %, p < 0.001); congestive heart failure (5 % vs 20 %, p < 0.001), previous MI (12 % vs 25 %, p < 0.001), anterior location of current MI (40 % vs 28 %, p < 0.002). Overall one-year Kaplan-Meier survival was 78 % for patients with versus 64 % for those without reperfusion therapy (p < 0.01). Cox multivariate analysis showed that reperfusion therapy was an independent predictor of survival (RR 0.71; 95% CI: 0.50-0.99), along with age (RR: 1.04, 95% CI: 1.02-1.07), anterior location of MI (RR: 2.14, 95 % CI: 1.64-2.80), history of stroke (RR: 1.81, 95 % CI: 1.25-2.61), and history of congestive heart failure (RR: 1.66, 95 % CI: 1.18-2.32). When the analysis was repeated after exclusion of the patients who underwent primary PTCA, treatment with IV thrombolysis was also associated with higher one-year survival, and thrombolysis was of borderline statistical significance in the Cox multivariate analysis (RR: 0.72, 95 % CI: 0.50-1.04, p=0.08). Conclusions: data from this large "real life" registry indicate that reperfusion therapy with either thrombolysis or primary PTCA is associated with improved one-year survival in patients over 70 years of age.

1050-43 **Gender Is an Independent Predictor of Both In-Hospital and One-Year Outcomes Following Primary Intervention for Acute Myocardial Infarction**

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Background: Prior studies have indicated that female gender contributes to worse prognosis from acute myocardial infarction (MI), elective percutaneous intervention (PCI), and coronary artery bypass grafting (CABG). However the impact of gender on outcomes following primary angioplasty for acute MI is not well established.
Methods: We evaluated the outcomes of 3401 patients from the PAMI studies receiving primary intervention for acute MI, of whom 27% were female. Clinical data, angiographic details and outcomes were evaluated.
Results: Females were older (66±12 vs 59±12, p=0.0001), more often diabetic (22% vs 14%, p=0.001), and hypertensive (57% vs 42%, p=0.001). They more often had prior congestive heart failure (3.4% vs 1.9%, p=0.009), and cerebrovascular events (9% vs 4%, p=0.001). Females were less often current smokers (36% vs 44%, p=0.001), had less incidence of prior CABG (2.6% vs 4.7%, p=0.010), prior MI (12% vs 15%, p=0.020), and prior PCI (7.7% vs 10.3%, p=0.021). Angiographically, patients were similar: initial % stenosis (98±6 vs 98±5, p=0.180), ejection fraction (48±12 vs 49±12, p=0.594), final % stenosis (15±17 vs 15±17, p=0.881) and TIMI flow pre (p=0.108) and post (p=0.747) procedure. Females had less multivessel disease (44% vs 49%, p=0.006). Females had higher in hospital death (4.6% vs 2.3%, p=0.001), death at 1 year (10% vs 6%, p=0.001) and target vessel revascularization (TVR) at 1 year (18% vs 13%, p=0.005). Adjusted for baseline differences, females remained at higher risk of in-hospital cardiovascular events including TVR, disabling stroke, reinfarction or death following primary PCI (8.7% vs 5.7%, p=0.001). This difference continues at 1 year (27% vs 19%, p=0.001). On multivariate analysis female gender is an independent predictor for in-hospital events (p=0.0025, OR=1.634, 95% CI=1.189-2.247) and remains predictive at 1 year (p=<0.0001, OR=1.553, 95%CI 1.258-1.916).
Conclusions: This data suggests that female gender is a significant independent predictor of major cardiovascular events at one year following primary PCI for acute MI. Further study is needed to determine if additional clinical and/or angiographic conditions also contribute to this difference.

1050-44 **Outcomes for Asian Indians Following Acute ST Elevation Myocardial Infarction: Results From the GUSTO Trials**

Venu Menon, Lilin She, Rabia Arshad, Anne S. Hellkamp, Sunil V. Rao, Judith S. Hochman, E Magnus Ohman, *St Lukes Roosevelt, NY, New York.*

Background: Relative outcomes following thrombolytic therapy for Asian Indians (AI) compared to Caucasians (C) have not been reported. Methods: We compared clinical outcomes in 475 AI enrolled in GUSTO-I (1990-3) GUSTO IIb (1993-5) and GUSTO-III (1995-7) and compared them to 54799 C. Results: AI were significantly younger, shorter and lighter than C (all P< 0.001). They were more likely to be male, have a history of diabetes but were less likely to be current smokers (all P < 0.001). Time to treatment, presenting heart rate, rates of hypertension and hypercholesterolemia were similar (all p = NS). Despite lower rates of angiography (37% vs 53%, p = 0.0001) and diminished left ventricular function in AI (47.7 ± 14.2 vs 51.5 ± 13.2, p = 0.004), distribution of 1-2-3 vessel disease were similar. Although rates of moderate/severe bleeding were comparable, AI had less strokes (0.21 vs 1.47%, p = 0.04). Overall 30 day and 1 year mortality for AI (6.99 vs 8.00% and 11.04% vs 11.36%) were similar as were rates of reinfarction and shock. Thirty day (OR 1.399, 95% CI 0.878, 2.230, p= 0.16) and 1 year mortality (OR 1.144, 95% CI 0.770, 1.699, p = 0.51) for AI remained similar to C after adjusting for age, gender, weight, height, systolic BP, Killip Class, heart rate, diabetes, hypertension, infarct location, smoking status, time to treatment, rates of previous MI, prior CABG, prior stroke and angina, as well as US location of enrollment. Amongst countries enrolling a large number of AI, observed 30 day mortality rates for AI in Canada (n = 200), USA (n = 108) and South Africa (n = 79) were 7.5%, 5.6% and 13.9% respectively. Conclusion: 30 day and 1 year mortality for AI are similar to C following acute ST elevation MI. Regional differences in outcome deserve further exploration.

POSTER SESSION

1051 Stable Ischemic Syndrome II: Therapy

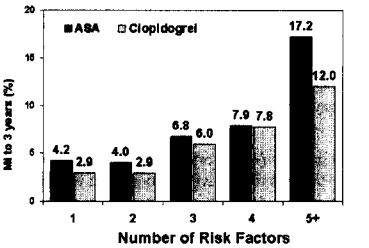
Sunday, March 17, 2002, 3:00 p.m.-5:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: 4:00 p.m.-5:00 p.m.

1051-27 **Predicting and Preventing Myocardial Infarction With Clopidogrel in Patients With Symptomatic Atherothrombosis: Results From CAPRIE**

Christopher P. Cannon, on behalf of the CAPRIE Investigators, *Brigham and Women's Hospital, Boston, Massachusetts.*

Background: Prevention of myocardial infarction (MI) is a major goal of therapy in patients (Pts) with documented atherothrombosis. Identification of Pts at higher risk of developing a subsequent MI may assist in selecting more aggressive therapy for these Pts to prevent of MI. Although prediction rules now exist for mortality, few prediction rules exist for MI. Also, factors that predict mortality (usually related to left ventricular failure) may not be the same as predictors of MI. **Methods:** In the CAPRIE trial 19,185 Pts with recent prior MI, stroke or documented peripheral arterial disease were randomized to receive clopidogrel or aspirin (ASA). We used multivariate (MV) analysis to develop a risk score for MI. **Results:** A new MI occurred in 5.04% of Pts treated with ASA vs. 4.20% for clopidogrel, a 19.2% relative reduction, p=0.008. MV predictors of MI were: Prior MI (p<0.0001), prior angina (p<0.0001), prior peripheral arterial disease (p<0.0001), highest quartile of creatinine (p<0.0001), diabetes (p=0.013), age ≥ 65 years (p=0.015), prior stroke (p=0.0497) and treatment with clopidogrel (O.R. = 0.80, adjusted p=0.0067). When stratifying by number of risk factors, the benefit of clopidogrel was an absolute 1.3% reduction in MI in Pts with 1-2 risk factors, and 5.2% in Pts with 5 or more risk factors.(Figure) **Conclusions:** Risk of MI can be predicted across a 4 fold range, from 4 to 17% over 3 years. Benefit of clopidogrel was seen in both low and high risk subgroups, supporting its use in a wide spectrum of patients.

MI Risk at 3 years based on # Risk Factors and Clopidogrel vs. ASA



1051-28 **Ramipril Prevents Major Cardiovascular Events in High-Risk Women: Results of the HOPE Trial**

Eva Lonn, Rosa Roccaforte, Qilong Yi, Jacqueline Bosch, Jeffrey Probstfield, Peter Sleight, Gilles Dagenais, Salim Yusuf, *McMaster University, Hamilton, Ontario, Canada.*

Background: It has been suggested based on subgroup analyses in heart failure (HF) and/or post myocardial infarction (MI) trials, that ACE inhibitors may be less effective in women than in men. These studies have generally included few women and were thus not adequately powered to assess the effects of ACE inhibitors in women. Furthermore, there are no data in women without HF and with preserved left ventricular ejection fraction (LVEF).
Methods: In the Heart Outcome Prevention Evaluation (HOPE) trial we enrolled a large number of women, who were at least 55 years of age and had documented vascular disease or diabetes and additional risk factor(s)without HF and with preserved LVEF. Patients were randomized to ramipril 10mg/day or placebo and mean follow up was 4.5 years. Treatment effects in women were evaluated as a preplanned subgroup analysis.
Results: There were 2,480 women. At baseline the placebo and ramipril groups were well balanced. Mean age was 66.5 years, 1,642 (66%) women had a history of CAD, 929 (37%) had prior MI, 273 (11%) had prior stroke or TIA, 1322 (53%) had diabetes and 1496 (60%) hypertension. Treatment with ramipril resulted in a significant reduction in the primary outcome, the composite of MI, stroke and CV death and in other outcomes of interest (Table). There was no difference (lack of statistical heterogeneity) in the magni-

tude of the effect of ramipril in women vs. men.
Conclusions: ACE inhibition with ramipril is highly effective in high-risk women without HF and with preserved LVEF.

Effect of Ramipril in Women

	Placebo (n=1201)	Ramipril (n=1279	RR (95% CI)	p
MI, stroke, CV death	179 (14.9%)	145 (11.3%)	0.76 (0.61-0.94)	0.01
MI	113 (9.4%)	105 (8.2%)	0.87 (0.67-1.14)	0.3
Stroke	58 (4.8%)	40 (3.1%)	0.61 (0.43-0.86)	0.004
CV Death	139 (11.6%)	118 (9.2%)	0.79 (0.62-1.02)	0.06
Revascularizations	173 (14.4%)	150 (11.7%)	0.81 (0.65-1.00)	0.05
Heart Failure	136 (11.3%)	117 (9.2%)	0.81 (0.63-1.03)	0.08
Worsening Angina	312 (26.0%)	275 (21.5%)	0.80 (0.68-0.94)	0.007
New Diabetes	27 (4.7%)	16 (2.7%)	0.58 (0.31-1.08)	0.08

1051-29 Effects of Vitamin E on Cardiovascular and Microvascular Outcomes in High-Risk Diabetic Patients

Eva Lonn, Hertzel Gerstein, Janice Pogue, Qilong Yi, Byron J. Hoogwerf, Jacqueline Bosch, Gilles Dagenais, Salim Yusuf, *McMaster University, Hamilton, Ontario, Canada.*

Background: Oxidative stress is an important mechanism of atherogenesis and microvascular damage in diabetes. Elevated protein kinase C (PKC) may also increase microvascular damage. Vitamin E is an antioxidant and decreases PKC activation.
Methods: We evaluated natural source Vitamin E (RRR-alpha-tocopheryl acetate) 400 IU/day vs. placebo in 3,654 high-risk persons with diabetes enrolled in the randomized controlled Heart Outcomes Prevention Evaluation (HOPE) trial. Median follow-up was 4.5 years. Data on major clinical outcomes were collected. Glycated hemoglobin (HbA1c) and serum creatinine were measured at baseline and yearly thereafter. Urinary albumin excretion was measured at baseline, 1 year and study end. Participants with albumin/creatinine ratio higher than 36 mg/mmol had 24 hour urine collections. Nephropathy was defined as 24-hour urinary albumin excretion of 300 mg or more or total protein excretion of 500 mg or more.
Results: Baseline characteristics were well balanced. Patients' mean age was 65 years, 3,572 had type 2 diabetes, 1,356 were women, 2,189 had known CAD, 244 had prior stroke, 678 peripheral arterial disease, 2,031 hypertension, 2,384 hypercholesterolemia. Major event rates (in %) were similar in the 2 groups (Table). Serial measurements of HbA1c, urinary albumin/creatinine ratio and serum creatinine were also similar in the 2 groups.
Conclusions: Vitamin E 400 IU/day has a neutral effect on CV outcomes and microvascular complications in high-risk diabetics.

CV and Microvascular Event Rates (in %)

	Placebo (n=1816)	Vitamin E (n=1838)	RR (95% CI)
MI, Stroke and CV Death	17.2	17.7	1.03 (0.88-1.21)
MI	11.5	11.5	1.01 (0.83-1.22)
Stroke	4.6	5.6	1.21 (0.91-1.62)
CV Death	8.0	7.7	0.97 (0.77-1.23)
Total mortality	12.8	11.9	0.93 (0.77-1.12)
Heart failure	4.2	4.6	1.11 (0.81-1.51)
Revascularizations	15.3	15.2	0.99 (0.82-1.17)
Overt Nephropathy	7.2	7.9	1.12 (0.88-1.44)
New Microalbuminuria	37.5	35.3	0.91 (0.79-1.03)
Retinal Laser Therapy	10.0	9.9	0.99 (0.81-1.22)

1051-30 Pharmacodynamic Interactions Between Tadalafil and Nitrates

Robert Kloner, Jeff Emmick, Alun Bedding, Dennis Humen, *Eli Lilly and Company, Erl Wood Manor, United Kingdom.*

Background: Tadalafil is a selective PDE5 inhibitor under regulatory review for the treatment of erectile dysfunction. Because sildenafil, another PDE5 inhibitor, is contraindicated in men taking nitrates, studies were undertaken to examine potential interactions between tadalafil and nitrates. **Methods:** Two double-blind, randomized, 3-way crossover studies were conducted in patients with stable angina to determine: 1) Study A - response to sublingual nitroglycerin (SL NG) administered 2 hours after tadalafil 5 or 10 mg or placebo (n=51); and 2) Study B - response after tadalafil 5 or 10 mg or placebo administered during daily long-acting nitroglycerin (LA NG) therapy (n=45). **Results:** The table shows the results for the primary endpoint, which was mean maximal change in standing systolic BP (MMCSBP).

Comparative Analysis of Standing MMCSBP Between Treatment Groups (mmHg)

	Tadalafil (10 mg)-Placebo		Tadalafil (5 mg)-Placebo	
	Mean Difference	Lower Bound of 95% CI	Mean Difference	Lower Bound of 95% CI
Study A (SL NG)	-3	-6	-8*	-12
Study B (LA NG)	-2	-6	0	-4

*Mean difference statistically significant based on non-inferiority analysis

Numbers of Patients with Standing SBP <85 mmHg (outliers)

	Placebo	Tadalafil 5 mg	Tadalafil 10 mg
Study A (SL NG)	1	13	11
Study B (LA NG)	0	0	6

There were no statistically significant differences in either study between tadalafil 5 or 10 mg and placebo in the sitting position. **Conclusions:** Tadalafil had minimal effects, relative to placebo, on mean blood pressure changes induced by either SL NG or LA NG. However, the frequency of outliers was higher in the tadalafil treatment groups, indicating that in a subset of patients, tadalafil augments the decrease in BP induced by nitrates. These results suggest that, as with sildenafil, tadalafil should not be used in combination with nitrates.

1051-45 Randomized Comparison of Exercise Training Versus PTCA/Stent in Stable Coronary Artery Disease: Effects on Clinical Status and Maximal Exercise Capacity

Katrin Conradi, Sven Möbius-Winkler, Claudia Walther, Peter Sick, Jiangtao Yu, Kai Kenziorra, Regine Kluge, Rainer Hambrecht, Gerhard Schuler, *University of Leipzig, Heart-Center, Department of Cardiology, Leipzig, Germany, University of Leipzig, Department of Nuclear Medicine, Leipzig, Germany.*

Introduction: In patients (pts) with stable coronary artery disease (CAD) regular exercise training has the therapeutic potential to improve physical work capacity (PWC). The aim of the present study was to evaluate the effects of exercise training in comparison to an interventional approach (PTCA and stent implantation) in pts with symptomatic CAD with respect to symptom-free PWC.
Methods: 100 male pts with stable CAD (amenable for PTCA/stent implantation) were prospectively randomized to either a training (T, n=50) or an intervention group (INT, n=50). Pts of the training group exercised 20 minutes daily on a bicycle ergometer whereas pts in the intervention group received initially a PTCA/stent implantation. At the beginning and after 6 months patients underwent a maximal symptom limited exercise stress test to assess PWC and maximal oxygen uptake (VO2 max).
Results: After 6 months pts of both groups demonstrated a significant improvement in clinical status from 1.33±0.13 to 0.6±0.11 (CCS-class, p<0.01 vs. begin) in T and 1.65±0.11 to 1.02±0.12 (p<0.01 vs. begin) in INT, respectively. Regular exercise training was associated with a significant increase in PWC (132±4.1 to 161±5 Watt; p<0.05 vs, INT) and peak oxygen uptake (22.2±0.6 to 25.3±0.9 mL/kg×min, p<0.05 vs. INT) in T, whereas INT showed no difference (119±3.4 to 124±4 Watt, n.s.; 20.8±0.6 to 21.5±0.7mL/kg×min, n.s.) Twenty-six pts of T and fifteen of INT were completely free of clinical symptoms after 6 months
Conclusions: These data suggest that in a selected daily physical exercise training seems to be a feasible alternative to an interventional approach with respect to clinical status and functional work capacity.

1051-46 Assessment of Reperfusion Therapy on Regional and Global Left Ventricular Function in Patients With Chronic Total Coronary Artery Occlusions

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Background: The regional and global ventricular function benefit achieved by percutaneous coronary intervention (PCI) with reperfusion of the artery supplying the infarct area in acute myocardial infarction (AMI) is well described. In addition, several trials indicate that PCI in AMI, reduces morbidity and mortality. Conversely, although the survival benefit of PCI in the setting of chronic total coronary occlusion (CTO) has recently been shown to be of little value, little is known of the potential effects on regional and global left ventricular function after late recanalization of CTO. This prospective study examined whether PCI improves regional and global left ventricular function (LVF) in CTO.
Methods: Patients (pts) having at least one coronary artery occluded for >6 weeks duration, were included in the study. Exercise Tl-201 myocardial perfusion scintigraphy (TMS), multiple gated acquisition (MUGA) ventriculography, and 2-dimensional echocardiography (Echo) were performed in each pt to assess both regional and global LVF before and 6 weeks after PCI. Paired sample t-tests were utilized for statistical analysis.
Results: Thirty-five pts were enrolled in the study. Fifteen pts were subsequently excluded because of inability to open the artery and one because of emergent angioplasty. In the remaining 19 pts (16 male and 3 female, mean age of 58±5 years) ejection fraction (EF) pre and post PCI, was 51±7% and 58±6% using Simpson's method (p<0.001) by Echo, and it was 45±1% and 53±1% (p<0.01) by MUGA, respectively. Echocardiographic wall motion score was 24±9 before and 15±6 (p<0.001) after PCI. Exercise perfusion score (21±1 and 14±1 [p=0.01]), rest perfusion score (15±1 and 12±1 [p=0.02]), and re-injection perfusion score (14±1 and 11±1 [p =0.07]) all also improved.
Conclusion: Percutaneous coronary reperfusion therapy significantly improved the regional and global left ventricular function in patients with chronic total coronary occlusion. Thus, although PCI may not benefit survival in CTO pts, improvement in ventricular function may provide important symptom benefits.

1051-47 Nitric Oxide Activity in Complex Atheromatous Plaques

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Background: Administration of L-arginine (LA) may stimulate the release of nitric oxide and improve myocardial ischemia.We sought to examine the effects of LA administration on coronary stenosis vasomotion in patients with coronary artery disease (CAD).
Methods: Intracoronary infusions of normal saline, the receptor mediated nitric oxide stimulant LA (50 and 150 µmol/min) and nitroglycerin (GNT) (250 mcg bolus) were administered in 15 patients with CAD and stable angina. Coronary stenoses were classified as smooth (smooth with regular borders) or complicated (irregular borders). The